Invasive cribriform carcinoma of the breast presenting as an erythematous papule on the nipple: a case report

Po-Yu Chen¹, Yu-Hsuan Ho¹, Chih-Jung Chen¹, and Chien-Shan Chiu¹

¹Taichung Veterans General Hospital

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Introduction:

Invasive cribriform carcinoma of the breast, initially described by Page et al in 1983 due to its predominant cribriform growth pattern in the invasive component and relatively favourable prognosis, is a rare type of breast carcinoma, accounting for 0.3 to 3.5% of primary breast carcinomas [1, 2]. ICC patients typically have a small tumour size, few axillary lymph node invasion, low distant metastasis rate, tumour with a high frequency of well differentiation, high ER and PR positive rates with rarely-observed human epidermal growth factor receptor 2 (HER2) amplification and a low proliferation index [3, 4, 5]. To date, studies of skin manifestations of invasive cribriform breast of the breast are notably scarce. We herein report a patient of ICC with a presentation as an erythematous papule on the nipple that no one has reported before.

Case history / examination:

A 71-year-old Asian woman visited our Department of Dermatology with a chief complaint of a reddish protruding skin lesion on the tip of her right nipple that had appeared for 6 months. Upon physical examination, the skin lesion was a solitary, well-demarcated papule, 0.2 by 0.2 cm in size, appearing centrally erythematous with violaceous in the periphery, fairly dome-shaped and firm [Figure 1a-c]. Besides, the papule was completely asymptomatic. The patient did not report any other abnormal symptoms. Her medical history was also unremarkable.

Differential diagnosis and investigations:

With these clues, a benign skin lesion had been impressed. Therefore, a local excision was performed to obtain a specimen of 0.7 by 0.5 by 0.3 cm in size. Biopsy results turned out to be pure invasive cribriform carcinoma of the breast (pure ICC), characterized by the invasive cribriform pattern comprising >90% of the lesion, in addition to mammary Paget’s disease (MPD) in the epidermis [Figure 2a-c]. Immunohistochemical tests showed positive expressions of both oestrogen and progesterone receptors [ER >95%, PgR >95%]. The reaction to HER2 (human epidermal growth factor receptor type 2) protein was negative [HER 2 (-)] [Figure 3a-c]. The Ki-67 labelling index was 5 %.

Treatment, outcome and follow-up:

In the diagnosis of pure ICC with MPD, she was referred to the Breast Surgery Department for further survey and treatment. Results on both CEA and CA15-3 levels were normal. Bilateral breast mammography (CC and MLO view) revealed segmental fine pleomorphic microcalcifications in the lower-inner quadrant of her right breast. These findings raise high suspicion for malignancy and are consistent with a classification of 4C in the BIRADS-US system. Breast ultrasound revealed two oval hypoechoic lesions with tiny calcifications which were 7.8 mm and 24.5 mm in size at the right breast near the areola. Whole body bone scan found no evidence of bone metastasis. With a previous biopsy pathology report revealing ICC and MPD, a full...
discussion was carried out with the patient. Finally, a simple mastectomy and sentinel lymph node biopsy were performed on her right breast.

With the right side simple mastectomy, pathology of the surgical specimen showed residual multifocal ductal carcinomas in situ. Both frozen sections of sentinel lymph nodes revealed no evidence of metastasis. The pathological TNM stage was pT1aN0 according to AJCC eighth edition. Further treatment plans for this patient included a five-year Tamoxifen therapy and regular follow-up at the Breast Surgery Department.

Discussion:

Based on the clinical features of the papule on her nipple, our initial impressions were benign skin lesions such as pyogenic granuloma, nipple adenoma, Spitz nevus and intradermal nevus. However, the pathologic diagnosis was pure ICC with MPD in the epidermis. Although ICC usually presents as an asymptomatic mass or may even be clinically occult[1, 3], the chance of ICC presenting as skin lesions cannot be ignored. The case reported by Katarzyna et al, in which ICC mimicked a breast abscess [6], along with our case of ICC presenting as a nipple papule, collectively demonstrates ICC’s potential to primarily manifest through skin lesions. To the best of our knowledge, ICC is a tumour having a more favourable prognosis than invasive breast carcinoma with less cribriform pattern and low grade invasive ductal carcinoma [11]. Despite favourable prognosis of ICC, there are still chances of aggressive behaviour or development into an advanced stage if left untreated long enough. Mishra et al reported a case of ICC with extensive perineural infiltration and lymphovascular invasion in a 58-year-old female; and Zhang et al also reported a case of pure ICC with bone metastasis when left untreated for 13 years[7, 8]. Therefore, such manifestation of a papule on the nipple, as in our case, may result in delayed diagnosis and treatment to ICC. It is crucial for dermatologists to have early awareness about skin manifestation of ICC and to avoid misdiagnosis.

Mammary Paget’s disease (MPD), first described by Sir Paget in 1874 as eczematous nipple and areola skin lesions, is a rare form of breast carcinoma comprising 1 to 3% of all breast cancers. Nearly all cases of MPD are affiliated with underlying breast carcinomas, typically located near the areola, and >90% are either ductal carcinomas in situ (DCIS) or invasive ductal carcinomas (IDC). Pathophysiologically, there are two main hypotheses proposed for the origin of MPD: the epidermotropic theory and the malignant transformation theory. The epidermotropic theory states that Paget cells originate from underlying breast carcinoma, and they migrate via the lactiferous ducts to the epidermis of the nipple. On the other hand, the malignant transformation theory states that Paget cells are malignant transformation of pluripotent keratinocyte stem cells or cells of apocrine gland ducts[9]. Although remains controversial, it is currently widely accepted that MPD is associated with underlying breast carcinoma, forming the concept based on the epidermotropic theory. In our case, ICC and MPD were diagnosed within the papular lesion on the nipple. This case stands out from >90% of cases in which mammary Paget’s disease was diagnosed exclusively with underlying DCIS or IDC. Furthermore, to the best of knowledge, only one publication focusing on radiologic characteristics of 52 MPD cases mentioned a case of invasive lobular and invasive cribriform carcinoma being diagnosed with mammary Paget’s disease presenting as a mass on mammography[10], but details or images were not provided. As to our case, it is worth knowing that the patient was diagnosed with multifocal DCIS at 1 cm near the right areola in the surgical specimen from simple mastectomy. In our opinion, it was the invasive cribriform carcinoma of the breast but not DCIS resulting in the mammary Paget’s disease in the epidermis of the papule [Figure 2c] as consistent with the epidermotropic theory. Although DCIS has been diagnosed near the areola, we believe that the chance of mammary Paget’s disease originating from the DCIS was slim. That is because malignant Paget cells were not seen at other parts of the nipple nor at the areola, but merely in the epidermis of the papule on the nipple. Furthermore, based on pathologic images, the gross pictures and the clinical manifestations of ICC and MPD, we believe that the invasive cribriform carcinoma of breast had caused the dome-shaped violaceous papule on the nipple, and mammary Paget’s disease contributed to the central erythematous part of the papular lesion [Figure 1a]. Undoubtedly, more studies are needed to bring attention to the skin manifestation of invasive cribriform carcinoma of the breast. As far as we know, no publication has ever reported on ICC with skin manifestation as a papule on the nipple. Also, no case has been reported with detailed images and descriptions regarding a pure ICC being diagnosed with MPD.
In this case report, we aim to bring awareness to skin manifestation of ICC.

References:


